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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,471	02/27/2004	Robert J. D'Amato	05213-3001 (13663.105082)	8547
20786	7590	08/12/2009	EXAMINER	
KING & SPALDING 1180 PEACHTREE STREET, NE ATLANTA, GA 30309-3521			BROOKS, KRISTIE LATRICE	
			ART UNIT	PAPER NUMBER
			1616	
			MAIL DATE	DELIVERY MODE
			08/12/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/789,471	Applicant(s) D'AMATO ET AL.	
	Examiner KRISTIE L. BROOKS	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 July 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/19/08; 5/28/09</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application

1. Claims 1-8 are pending.
2. Receipt and consideration of Applicants amendments/remarks filed on July 3, 2008 is acknowledged.
3. Rejections not reiterated from the previous Office Action are hereby withdrawn.
The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.
4. Upon further consideration by the Examiner, **new** grounds of rejection are presented below.

New Grounds of Rejection

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

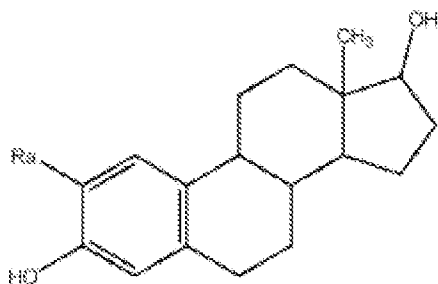
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

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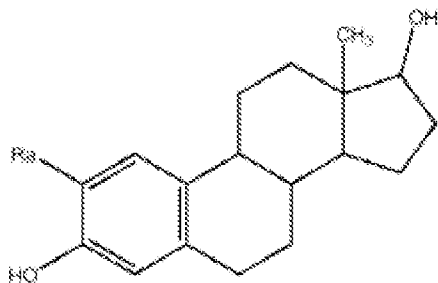
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-8 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 7,081,477.

The instant claims are drawn to a method of inhibiting neovascularization associated with angiogenesis in a mammal comprising administering to the mammal a neovascularization-inhibiting amount of a compound of the formula:



Claims 1-2 of U.S. Patent No. 7,081,477 are drawn to a method of treating angiogenesis mediated cancer in a human or an animal comprising administering to the human or animal an amount of a compound effective to treat the cancer, the compound having the formula:



Although the conflicting claims are not identical, they are not patentably distinct from each other because they both encompass treating angiogenesis in a mammal. The instant invention differs from the cited patent by recitation of "treating neovascularization associated with angiogenesis". However, the treatment of neovascularization is limited to the process involving angiogenesis. Therefore, the method claimed in US Patent No. 7,081,477 is a species of the genus of the method encompassed by the instant claims, and as such, is not patentably distinct from the instant invention.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

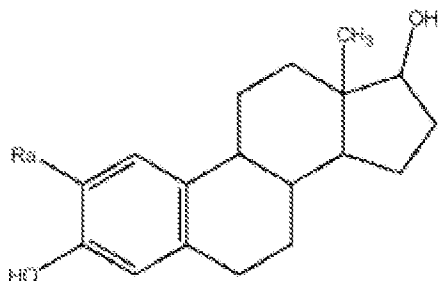
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 1-2, 4-5, and 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seegers et al., The cytotoxic effects of estradiol-17, catecholestradiols and methoxyestradiols on dividing MCF-8 and HeLa cells, *The Journal of Steroid Biochemistry*, 32(6), pp.797-809, 1989, in view of Liehr et al., Carcinogenicity of catechol estrogens in Syrian hamsters, *The Journal of Steroid Biochemistry*, 24(1), 353-356, 1986.

Applicant claims a method of inhibiting neovascularization associated with angiogenesis in a mammal comprising administering to the mammal a neovascularization-inhibiting amount of a compound of the formula:



Determination of the scope and content of the prior art

(MPEP 2141.01)

Seegers et al. teach the antimitotic properties of 2-methoxyestradiol (2-MEOE2) in dividing MCF-8 and HeLa cells (see the abstract and pages 807-809). Seegers et al.

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also teach 2-methoxyestradiol holds the greatest potential as an anti-tumor agent, because of its toxic effects on dividing malignant MCF-8 and HeLa cells (see column 2, first paragraph).

**Ascertainment of the difference between the prior art and the claims
(MPEP 2141.02)**

Seegers et al. do not exemplify administration to a mammal. This deficiency is cured by the teachings of Liehr et al.

Liehr et al. teach estrogen and estradiols induce renal carcinoma in male Syrian hamsters (see the abstract). Animals treated with 2-methoxyestradiol did not develop renal carcinoma and stimulation of tumor growth by 2-methoxyestradiol was not detected (see the abstract, Table 2 on page 354, carcinogenic activity, and the discussion on page 355).

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

One of ordinary skill in the art would have been motivated to administer 2-methoxyestradiol because of its known anti-mitotic properties on human cells, as suggested by Seegers et al. Furthermore, it is known that 2-methoxyestradiol was not

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found to be carcinogenic nor cause tumor growth in mammals, as suggested by Liehr et al.

Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to administer 2-methoxyestradiol to a mammal for the purpose of obtaining the therapeutic benefits from the compound, without the carcinogenic effects found in some estrogen compounds.

With regard to the preamble, “treating neovascularization associated with angiogenesis” in claim 1, it is the Examiner’s position that since 2-methoxyestradiol has anti-mitotic properties (which results in inhibiting cell mitosis, thereby inhibiting cell proliferation of new blood vessels (angiogenesis)) as well as potential as an antitumour agent, the method of use is encompassed by such administration, especially in absence of evidence to the contrary.

With regard to the limitation, “wherein the neovascularization is ocular neovascularization”, it is the Examiner’s position that one of ordinary skill in the art can reasonably assume that 2-methoxyestradiol can inhibit mitosis in any tissue, including ocular tissue, and thus, the limitation is met, especially in absence of evidence to the contrary.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

Response to Arguments

Applicant's arguments filed July 3, 2008 have been fully considered but they are not persuasive.

Applicant's arguments with respect to claims 1-8 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

9. Claims 3 and 6 are objected to as being dependent upon a rejected base claim, but would be allowable, pending a search update at the time of allowance, if rewritten in independent form, including all of the limitations of the base claim and any intervening claims.

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kristie L. Brooks whose telephone number is (571) 272-9072. The examiner can normally be reached on M-F 8:30am-6:00pm Est..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

KB

/Mina Haghighatian/
Primary Examiner, Art Unit 1616